Amendments to the Claims/Listing of Claims

Please amend claims 1, 2, 4, and 7 as follows. This listing of claims will replace all prior versions, and listings, of claims in the application.

1. (Currently Amended) A method for developing **an improved** ligand**[[s]]** binding to PDE5A, comprising

identifying as molecular scaffolds one or more compounds that bind to a binding site of PDE5A;

determining the orientation of at least one molecular scaffold in **a** co-crystal**[[s]]** with PDE5A; **[[and]]**

identifying chemical structures of said **at least one** molecular scaffold**[[s]]**, that, when modified, alter the binding affinity or binding specificity or both between the molecular scaffold and PDE5A; **[[and]]**

synthesizing a ~~ligand~~ **compound** wherein one or more of the chemical structures of the molecular scaffold is modified ~~to provide a ligand that binds to PDE5A with altered binding affinity or binding specificity or both~~**; and**

testing the compound for binding to PDE5A, wherein binding with increased affinity or specificity is indicative that the compound is an improved ligand.

2. (Currently Amended) The method of claim 1, wherein said molecular scaffold **binds to the binding site of PDE5A with a dissociation constant of 1 μM to about 1 mM** ~~is a weak binding compound~~.

3. (Original) The method of claim 1, wherein said molecular scaffold binds to a plurality of phosphodiesterases.

4. (Currently Amended) A method for developing **an improved** ligand**[[s]]** specific for PDE5A, comprising

identifying a compound that binds to a plurality of phosphodiesterases;

determining the orientation of the compound in a co-crystal with PDE5A;

identifying chemical structures of the compound, that, when modified, alter the binding specificity between the compound and PDE5A;

modifying one or more of the chemical structures of the compound to provide a derivative; and

determining ~~**whether a**~~ **the specificity with which the** derivative ~~**of said compound has**~~ **binds PDE5A, wherein binding with** greater specificity for PDE5A than said compound **is indicative that the derivative is an improved ligand**.

5. (Original) The method of claim 4, wherein said compound binds to PDE5A with an affinity at least 10-fold greater than for binding to any of said plurality of phosphodiesterases.

6. (Original) The method of claim 5, wherein said compound interacts with at least one conserved PDE5A active site residue.

7. (Currently Amended) The method of claim 4, wherein said compound binds **[[weakly]]** to said plurality of phosphodiesterases **with a dissociation constant of 1 μM to about 1 mM**.

8. (Original) The method of claim 4, wherein said plurality of phosphodiesterases comprises PDE5A and PDE6.

9. (Original) The method of claim 4, wherein said plurality of phosphodiesterases comprises PDE5A and PDE11.

10. (Withdrawn) A method for identifying potential PDE5A binding compounds, comprising

identifying a molecular scaffold that binds to PDE5A; and

fitting at least one electronic representation of a compound in an electronic representation of a PDE5A binding site, wherein said compound is a derivative of said molecular scaffold.

11. (Withdrawn) The method of claim 10, wherein said electronic representation of a PDE5A binding site is defined by atomic structural coordinates set forth in Table 1.

12. (Withdrawn) The method of claim 10, comprising

removing a computer representation of a compound complexed with PDE5A and fitting a computer representation of a compound from a computer database with a computer representation of the active site of PDE5A; and

identifying compounds derived from said molecular scaffold that best fit said active site based on favorable geometric fit and energetically favorable complementary interactions as potential binding compounds.

13. (Withdrawn) The method of claim 10, comprising

modifying a computer representation of a compound complexed with PDE5A by the deletion or addition or both of one or more chemical groups;

fitting a computer representation of a compound derived from said molecular scaffold from a computer database with a computer representation of the active site of PDE5A; and

identifying compounds derived from aid molecular scaffold that best fit said active site based on favorable geometric fit and energetically favorable complementary interactions as potential binding compounds.

14. (Withdrawn) The method of claim 10, comprising

removing a computer representation of a molecular scaffold or a derivative compound thereof complexed with PDE5A and; and

searching a database for compounds having structural similarity to said molecular scaffold or derivative compound using a compound searching computer program or replacing portions of said compound with similar chemical structures using a compound construction computer program.

15. (Withdrawn) The method of claim 10, wherein said compound complexed with PDE5A is non-hydrolyzable cGMP analog.

16. (Withdrawn) The method of claim 10, wherein said fitting comprises determining whether a said compounds will interact with one or more of conserved PDE5A active site residues.

17. (Withdrawn) A method for attaching a PDE5A binding compound to an attachment component, comprising

identifying energetically allowed sites for attachment of a said attachment component on a phosphodiesterase binding compound; and

attaching said compound or derivative thereof to said attachment component at said energetically allowed site.

18. (Withdrawn) The method of claim 17, wherein said attachment component is a linker for attachement to a solid phase medium, and said method further comprises attaching said compound or derivative to a solid phase medium through a linker attached at a said energetically allowed site.

19. (Withdrawn) The method of claim 17, wherein said phosphodiesterase comprises conserved residues matching at least one conserved PDE5A active site residues.

20. (Withdrawn) The method of claim 18, wherein said linker is a traceless linker.

21. (Withdrawn) The method of claim 18, wherein said phosphodiesterase binding compound or derivative thereof is synthesized on a said linker attached to said solid phase medium.

22. (Withdrawn) The method of claim 21, wherein a plurality of said compounds or derivatives are synthesized in combinatorial synthesis.

23. (Withdrawn) The method of claim 18, wherein attachment of said compound to said solid phase medium provides an affinity medium.

24. (Withdrawn) The method of claim 17, wherein said attachment component comprises a label.

25. (Withdrawn) The method of claim 24, wherein said label comprises a fluorophore.